EXHIBIT H — PROCEDURAL RECORD

VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain (2017) and Evidence Synthesis Report — selected pages

Source: VA FOIA Request No. 25-25897-F production • Submitted with public comment, HHS FR Doc. 2026-11602 (91 FR 35221)

CPG = VA/DoD Clinical Practice Guideline (2017), cited by production page stamp "Page X of 198." ESR = Evidence Synthesis Report (The Lewin Group), cited by production page stamp "Page X of 353." Tabs are grouped by the section of the public comment they support; tab numbers are identifiers, not sequence.

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H-03	CPG p. 119	GRADE framework permitting strong recommendations even when evidence quality is low
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H-15	CPG p. 67	Future Research section: outcome evidence on tapering processes still needed
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H-17	ESR p. 332	Literature searches conducted by ECRI Institute information specialists

Highlighting added by submitter for reviewer convenience; underlying documents unaltered. Full document set available from the VA FOIA office under Request No. 25-25897-F.

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PART 1 — Evidence base for tapering (supports Policy Idea 2.1)

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CPG = Clinical Practice Guideline | ESR = Evidence Synthesis Report

  - Be aware of interactions between methadone and other drugs that may prolong QTc interval or slow the elimination of methadone, and educate patients about potential drug interactions
- Conservative dosing
  - Methadone should not be initiated in opioid-naïve patients in the outpatient setting
  - Primary care clinicians should never rotate from another opioid to methadone without guidance from an experienced clinician regarding the starting dose of methadone
  - When initiating or increasing dosage, close follow-up is recommended (e.g., within five to seven days) to assess signs of methadone toxicity, such as excess sedation or delirium
  - Wait at least one week on a particular dose of methadone before increasing dosage of methadone to make sure that the full effects of the previous dosage are evident

Recommendations

14. We recommend tapering to reduced dose or to discontinuation of long-term opioid therapy when risks of long-term opioid therapy outweigh benefits.
    (Strong for | Reviewed, New-added)

    Note: Abrupt discontinuation should be avoided unless required for immediate safety concerns.

15. We recommend individualizing opioid tapering based on risk assessment and patient needs and characteristics.
    (Strong for | Reviewed, New-added)

    Note: There is insufficient evidence to recommend for or against specific tapering strategies and schedules.

Discussion

Clinicians should reassess the use of LOT in all patients currently receiving the therapy and consider tapering or discontinuing opioids in all patients on LOT when the risks exceed the benefits of therapy. Treatment of chronic pain with LOT in general is associated with considerable risk and must be justified by attainment of benefit that outweighs those risks in any individual patient. Non-pharmacologic therapies and non-opioid pharmacologic therapies are preferred and should be optimized. See Recommendation 1 for additional information on recommended treatments for chronic pain.

Observational studies (not included in the evidence review) suggest that when opioids are tapered or discontinued within the context of a multi-modal pain rehabilitation care plan, patients can experience an improvement in their pain, function, and mood.[170,171] Although the confidence in the quality of the evidence was low, the Work Group's determination that the benefits of individualized tapering of OT (when risks of LOT outweigh benefits) greatly outweigh the harms of tapering, as well as their consideration of individual patients' values and preferences, supported strong recommendations.

Indications for Tapering

If risks of OT outweigh benefits, OT should be tapered to a reduced dose or tapered to discontinuation. In the context of shared decision making, patient-specific goals, values, and preferences, the following should

III. Recommendations

The following recommendations were made using a systematic approach considering four domains as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach as detailed in the section on Methods and Appendix E. These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications, as appropriate (e.g., resource use, equity, acceptability).

Given the relevance of all four domains in grading recommendations, the Work Group encountered multiple instances in which confidence in the quality of the evidence was low or very low, while there was marked imbalance of benefits and harms, as well as certain other important considerations arising from the domains of values and preferences and/or other implications. In particular, the harms due to the potential for severe adverse events associated with opioids, particularly overdose and OUD, often far outweigh the potential benefits. As such, in accounting for all four domains, these factors contributed to Strong recommendations in multiple instances.

#	Recommendation	Strength*	Category†
Initiation and Continuation of Opioids			
1.	a) We recommend against initiation of long-term opioid therapy for chronic pain. b) We recommend alternatives to opioid therapy such as self-management strategies and other non-pharmacological treatments. c) When pharmacologic therapies are used, we recommend non-opioids over opioids.	a) Strong against b) Strong for c) Strong for	Reviewed, New-replaced
2.	If prescribing opioid therapy for patients with chronic pain, we recommend a short duration. Note: Consideration of opioid therapy beyond 90 days requires re-evaluation and discussion with patient of risks and benefits.	Strong for	Reviewed, New-added
3.	For patients currently on long-term opioid therapy, we recommend ongoing risk mitigation strategies (see Recommendations 7-9), assessment for opioid use disorder, and consideration for tapering when risks exceed benefits (see Recommendation 14).	Strong for	Reviewed, New-replaced
4.	a) We recommend against long-term opioid therapy for pain in patients with untreated substance use disorder. b) For patients currently on long-term opioid therapy with evidence of untreated substance use disorder, we recommend close monitoring, including engagement in substance use disorder treatment, and discontinuation of opioid therapy for pain with appropriate tapering (see Recommendation 14 and Recommendation 17).	a) Strong against b) Strong for	Reviewed, Amended
5.	We recommend against the concurrent use of benzodiazepines and opioids. Note: For patients currently on long-term opioid therapy and benzodiazepines, consider tapering one or both when risks exceed benefits and obtaining specialty consultation as appropriate (see Recommendation 14 and the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders).	Strong against	Reviewed, New-added

Table E-6. Evidence to Recommendation Framework

Decision Domain	Judgment
Balance of desirable and undesirable outcomes	
▪ Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa? ▪ Are the desirable anticipated effects large? ▪ Are the undesirable anticipated effects small? ▪ Are the desirable effects large relative to undesirable effects?	Benefits outweigh harms/burden Benefits slightly outweigh harms/burden Benefits and harms/burden are balanced Harms/burden slightly outweigh benefits Harms/burden outweigh benefits
Confidence in the quality of the evidence	
▪ Is there high- or moderate quality evidence that answers this question? ▪ What is the overall certainty of this evidence?	High Moderate Low Very low
Values and preferences	
▪ Are you confident about the typical values and preferences and are they similar across the target population? ▪ What are the patient's values and preferences? ▪ Are the assumed or identified relative values similar across the target population?	Similar values Some variation Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	
▪ Are the resources worth the expected net benefit from the recommendation? ▪ What are the costs per resource unit? ▪ Is this intervention generally available? ▪ Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? ▪ Is there lots of variability in resource requirements across settings?	Various considerations

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which combines the four domains.[68] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low.[256] In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

Key Question 9: What is the safety and effectiveness of different tapering strategies and schedules?

Summary of Evidence Base

Based on our searches and inclusion criteria for this report, we identified two studies that were included as evidence for this key question. The identified studies, described below, addressed the safety and effectiveness of different tapering strategies and schedules in patients suffering from chronic pain.

- Our searches identified two studies, a prospective longitudinal study (Wang et al. 2011[1]) and a randomized controlled trial (RCT; Nomura et al. 2011[2]) as evidence for this key question.
- Wang et al. 2011[1] focused on the changes in pain sensitivity during opioid tapering and withdrawal in chronic lower back pain (cLBP) patients on long-term opioid therapy. The findings suggested that long-term use of opioids did not reduce pain sensitivity. However, opioid tapering did induce brief hyperalgesia.
- Nomura et al. 2011[2] evaluated the safety and efficacy of conversion methods in chronic cancer pain patients. Overall, authors reported an excellent safety profile and sustained efficacy for the 6-h conversion method compared with the 12-h conversion method. This was performed in the form of continuous intravenous infusion conversion to transdermal fentanyl using a two-step tapering approach.
- Both studies[1,2] received a Very low quality rating for their outcomes due to serious study limitations and imprecision in their findings based on the GRADE criteria.

Overview of Evidence Base

Our searches of the literature identified one prospective longitudinal study and one RCT that considered the evidence for the safety and effectiveness of different tapering strategies and schedules in patients with chronic pain. The prospective longitudinal study by Wang et al. 2011[1] enrolling 98 patients, investigated pain sensitivity after tapering of long-term opioid use in a homogeneous cLBP patient population. Pain sensitivity was monitored for 6 months.[1] The double-blinded RCT by Nomura et al. 2011 evaluated 87 patients and compared the safety and efficacy of a 12-hour conversion method versus a 6-hour conversion method in chronic cancer pain management. Patients had follow-ups at 6, 12, 18, 24 and 48 hour intervals.[2] Studies excluded as evidence for this key question and reasons for their exclusion are presented in Table 4 of the Appendix.

Study Quality Rating

The Wang et al. 2011[1] longitudinal study was rated Fair as the authors used appropriate attention to confounders in analysis but had less than 80% follow-up at 6 months. Nomura et al. 2011[2] was rated Fair mostly due to lack of intent-to-treat analysis. The study however used adequate randomization and allocation concealment methods, and matching baseline characteristics based on USPSTF criteria.

Overview of Study, Patient, and Intervention Characteristics

Below we provide a brief description of the study, patient, and intervention characteristics of the studies that make up the evidence base for this key question. Additional information is provided in Table 2.

The Wang et al. 2011[1] study investigated the long-term (17 months) effects of opioid analgesics on pain sensitivity and evaluated the changes in pain sensitivity during opioid tapering and withdrawal in patients currently using opioids compared with two groups of non-opioid users. The patient population included mostly non-elderly (mean age 47.6 years) women (54.1%) diagnosed with chronic myofascial LBP. All patients were on active opioid therapy treatments, defined as intake of a morphine equivalent dose of at least 30 mg per day every day for more than 3 months. The authors used the quantitative sensory testing (QST) technique to assess pain sensitivity at 1 day before (T1), 3 weeks after (T2), and 6 months after the start of opioid tapering (T3) in 35 patients with both cLBP and opioid medication (OP). The comparison groups included 35 opioid-naïve (ON) cLBP patients who had not used opioids for 3 months prior to baseline, and 28 healthy controls (HC) with neither pain nor opioid intake. Tapering was performed by reducing the dosage of opioid preparation by half every 3 days until the patients became opioid clean. All patients had stopped the use of opioids by T2.

The other study was a double-blinded RCT (Nomura et al. 2011)[2] designed to compare the safety and efficacy of the conversion from continuous intravenous infusion to transdermal fentanyl using two-step tapering of the continuous intravenous infusion in the 12 h (12-h method) or in the 6 h (6-h method) conversion. The study included mostly elderly patients (mean age 60 years) who were diagnosed with chronic cancer pain. Majority of the patients were men (70.1%) with assessable pain intensity being pretreated with continuous intravenous fentanyl. The mean dosages of the applied fentanyl transdermal patch (post randomization) were 23.3±13.3 μg/h (range, 12.5 to 100 μg/h) in the 12-h group and 28.3±21.4 μg/h (range, 12.5 to 100 μg/h) in the 6-h group. Patients were randomly allocated to one of the conversion method groups. In the 12-h group, fentanyl was administered using the 12-h method, and saline was administered using the 6-h method. In the 6-h group, fentanyl was administered using the 6-h method, and saline was administered using the 12-h method. Pain intensity and bolus use frequency between the two treatment methods were assessed.

Outcomes and Synthesis of Results

Below we provide an overview of the main findings of each study. Additional information and results are provided in Table 2.

Tapering Intervention in Chronic Lower Back Pain Patients on COT

Pain sensitivity (heat pain thresholds): Significant differences were reported in one study (Wang et al. 2011[1]) among the three groups at all three time points (T1: p=0.001, T2: p=0.015, T3: p=0.008) but not between the two cLBP patient groups (i.e. opioid medication group and opioid naïve group). At T3 (6 months after start of tapering), the heat pain thresholds of cLBP and opioid medication patients still remained lower than healthy controls (p=0.017), while those of cLBP and opioid naïve patient group were normalized.

Pain sensitivity (cold pain thresholds): cLBP and opioid medication patients showed lower cold pain thresholds at T2 (at 3 weeks) than cLBP and opioid naive patients and healthy controls.[1]

Pain sensitivity (warm stimuli): One study reported that compared with T1 (1 day before start of tapering), cLBP and opioid medication patients reacted to warm stimuli significantly faster at T2 (at 3 weeks) (p=0.029), while cLBP and opioid naïve patients did not change their pain profile. At T3 (6 months after start of tapering), cLBP and opioid medication patients showed a further increase in speed of reaction to warm stimuli (p=0.01) and a further lowering of cold pain thresholds (p=0.026) relative to T2.[1]

Adverse events: Nausea, weakness, increased sweating, and sleep disturbance were reported during week 1.[1]

Statistically significant correlations were found between sensation of warmth in the hand and both age (r=0.308, p=0.015) and sex (r=0.271, p=0.003). Moderate correlations were observed with NRS scores and thermal sensation. No correlations were determined between QST values and depression, pain duration, opioid dose, or opioid duration.[1]

The authors concluded that long-term use of opioids did not reduce pain sensitivity in cLBP patients.

Tapering Conversion Intervention in Chronic Cancer Pain Patients

Pain intensity: No significant increases in pain intensity were found in both groups. In the 12-h group, significant decreases in pain intensity were identified at 6h and 12-h compared with that prior to application of the fentanyl patch (6-h 95% CI: 0.17 to 0.63; p=0.003; 12-h 95% CI: 0.23 to 0.84; p=0.003). There were no significant decreases in pain intensity in the 6-h group (p>0.05).[2]

Bolus use: No significant between group differences were reported.[2]

Adverse events/toxicity: A higher incidence of opioid-related adverse events above baseline was found in the 12-h conversion group compared with the 6-h conversion group (95% CI: 0.01 to 0.55; p=0.002). Similarly, significant differences in the incidence of adverse events was observed in the 12-h method group versus the 6-h method group (12-h group=25.6%, 6-h group=2.3%; 95% CI: 0.01 to 0.55; p=0.002). Adverse events, which were considered opioid-related, led to early discontinuations for 16% of patients in the 12-h method group. Grade 3 or more adverse events occurred in seven patients in the 12-h group (p=0.005).[2]

The authors reported an "excellent safety profile" and sustained efficacy for the 6-h conversion method.

Overall Quality of Evidence Rating

- Table 1 presents the overall quality ratings for outcomes reported in the studies included as evidence for this key question. The two studies included a prospective longitudinal analysis (Wang et al. 2011[1]) and a RCT (Nomura et al. 2011[2]). The evidence presented in Wang et al. 2011[1] received a Very low rating for the outcome of pain sensitivity due to very serious study limitations (non-RCT study design and less than 80% follow-up) and very serious imprecision related to both lack of precision in reporting statistical outcomes (only p values were reported) and the evidence base consisting of only one trial with small sample size. The evidence presented in Nomura et al. 2011[2] received a Very low rating for the outcomes of pain intensity, bolus use and adverse events due to very serious study limitations related to a lack of intent-to-treat analysis and serious imprecision related to the evidence base consisting of only one trial with small sample size.

Appendix A. Evidence Tables

Table 2. Individual Studies

Study Details	Patients/Interventions	Intervention/Treatment	Outcomes/Results
Reference: Wang et al. 2011[1] **Country:** Germany **Study Design:** Prospective, longitudinal study **Purpose:** To investigate pain sensitivity in a homogeneous patient population (chronic low back pain [cLBP] patients only) after tapering of long-term (17 months) opioid use and to monitor the changes in pain sensitivity for 6 months **Quality Rating:** Fair Authors used appropriate attention to confounders in analysis but the study had less than 80% follow-up. Lack of precision in reporting statistical findings (p-values only).	**Number of Patients:** 98 patients (35 patients with both cLBP and opioid medication [OP], 35 opioid-naïve cLBP patients [ON], and 28 individuals with neither pain nor opioid intake [HC]) **Diagnosis:** cLBP **Age (Years):** Mean 47.6 years **Gender:** Women 54.1% **Inclusion Criteria:** Study included patients with cLBP who were 1) aged between 20 and 70 years; 2) had a history of at least 6 months of chronic myofascial LBP without radicular sensory or motor deficits or radicular pain symptoms (herniation or disc protrusion excluded by magnetic resonance imaging), but sick leave amounting to less than 6 months within the 12 months immediately before enrollment in this study (grade II chronification according to von Korff); 3) defined opioid therapy as intake of a morphine equivalent dose of at least 30 mg per day every day for more than 3 months. Non-opioid pain medication in the group of opioid-naïve patients was allowed. **Exclusion Criteria:** The exclusion criteria for both patient groups were: 1) sensory deficits because of diabetes, alcoholic neuropathy, spinal stenosis, or severe thyroid, liver, or kidney disease; 2) interventional pain management procedures that might alter QST responses, including neuraxial or local anesthetic block, within the previous 3 months; 3) major psychiatric disorders requiring recent hospitalization, such as schizophrenia or psychosis; and 4) infection or acute injury at the QST site.	**Treatment:** The dosage of opioid preparation was halved every 3 days until the patients became opioid clean. Data from patients who remained opioid clean at 6 months was used for statistical analysis (group 1, *N*=17; group 2, *N*=22, group 3, *N*=18). **Primary Outcome:** Sensitivity (thermal sensation and thermal pain thresholds in low back and non-dominant hand) was measured by quantitative sensory testing (QST) at 1 day before (T1), 3 weeks after (T2), and 6 months after the start of opioid tapering (T3) **Note:** For the standardized data analysis, they study used the following conversion ratios between an oral dose of morphine and other opioid analgesics: 1 mg morphine = 0.65 mg oxycodone, 0.25 mg methane, 5 mg tilidine, 0.01 mg fentanyl, 0.13 mg hydromorphone, 5 mg tramadol. **Follow-up:** 6 months	**Pain Sensitivity (Heat Pain Thresholds):** Significant differences in heat pain thresholds were found among the three groups at all three time points (T1: p=0.001, T2: p=0.015, T3: p=0.008), however no differences were reported at any time point between the two patient groups (OP and ON) At T3, the heat pain thresholds of cLBP and opioid medication patients (OP) still remained lower than HC (p=0.017), while those of cLBP and opioid naïve patients (ON) were normalized. **Pain Sensitivity (Cold Pain Thresholds):** cLBP and opioid medication patients showed lower cold pain thresholds at T2 than cLBP and opioid naive patients and HC. **Pain Sensitivity (Warm Stimuli):** Compared with T1, cLBP and opioid medication patients reacted to warm stimuli significantly faster at T2 (p=0.029), while cLBP and opioid naïve patients did not change their pain profile. At T3, cLBP and opioid medication patients showed a further increase in speed of reaction to warm stimuli (p=0.01) and a further lowering of cold pain (p=0.026) relative to T2. Statistically significant correlations were determined between sensation of warmth in the hand and both age (*r*=0.308, p=0.015) and sex (*r*=0.271, p=0.003). Moderate correlations were observed with NRS scores and thermal sensation. No correlations were observed between QST values and depression, pain duration, opioid dose, or duration. **Adverse Events:** Nausea, weakness, increased sweating, and sleep disturbance were commonly reported during week 1. The authors concluded that long-term use of opioids did not reduce pain sensitivity in cLBP patients; though opioid tapering induced brief hyperalgesia.

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PART 2 — Risk-mitigation precedent and efficacy (supports Policy Idea 2.2)

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- **Co-administration of a drug capable of inducing fatal drug-drug interactions:** Providers should carefully rule out and avoid potential drug interactions prior to initiating LOT. For example, the following combinations are dangerous:[66]
  - Opioids with benzodiazepines (compared to patients with no prescription, the odds ratio [OR] and 95% confidence interval [CI] for drug-related death was OR: 14.92, 95% CI: 7.00-31.77 for patients who filled a prescription for opioids and benzodiazepines; OR: 3.40, 95% CI: 1.60-7.21 for patients who filled only an opioid prescription, and 7.21, 95% CI: 3.33-15.60 for patients who filled only a benzodiazepine prescription) (see Recommendation 5) [66,67]
  - Fentanyl with CYP3A4 inhibitors
  - Methadone with drugs that can prolong the QT interval (the heart rate's corrected time interval from the start of the Q wave to the end of the T wave) (e.g., CYP450 2B6 inhibitors)
- **QTc interval >450 ms for using methadone:** Unlike most other commonly used opioids, methadone has unique pharmacodynamic properties that can prolong the QTc interval (the heart rate's corrected time interval from the start of the Q wave to the end of the T wave) and precipitate torsades de pointes, a dangerous or fatal cardiac arrhythmia. Patients who may be at risk include those with other risk factors for QTc prolongation, current or prior electrocardiograms (ECGs) with a prolonged QTc >450 ms, or a history of syncope. Therefore, ECGs before and after initiating methadone are highly advised (see Methadone Dosing Guidance).
- **Evidence for or history of diversion of controlled substances:** The clinician should communicate to patients that drug diversion is a crime and constitutes an absolute contraindication to prescribing additional medications. Because suspicion is subjective and may be based on impression, bias, or prejudice, it is important that providers who suspect diversion base treatment plans on objective evidence. Suspicions may be confirmed by a negative mass spectrometry/liquid chromatography UDT for the substance being prescribed in the absence of withdrawal symptoms in someone who is receiving opioids. A negative UDT for the prescribed opioid could also by itself be a sign of diversion. Signs of diversion may also include frequent requests for early refills or atypically large quantities required to control pain. Routine UDT, however, may not reliably detect synthetic opioids (e.g., methadone, fentanyl, tramadol) or semi-synthetic opioids (e.g., oxycodone, hydrocodone, hydromorphone). When there is evidence that the patient is diverting opioids, discontinue opioids according to Recommendations 14 and 15 and assess for underlying OUD and/or psychiatric comorbidities. Consultation with a pain specialist, psychiatrist, or SUD specialist may be warranted. Also consider consultation with local risk management and/or counsel. For patients with OUD, keep in mind that sudden discontinuation of opioids due to suspected diversion may place them at high risk for illicit opioid use and resulting opioid overdose (see Recommendation 17).
- **Intolerance, serious adverse effects, or a history of inadequate beneficial response to opioids:** Serious harm may occur should patients be prescribed additional (or different) opioids if prior administration of opioids led to serious adverse effects or was not tolerated. It is also inadvisable to prescribe opioids to patients who already have had an adequate opioid trial (of

A number of studies suggest certain chronic pain conditions represent an independent risk factor for suicide.[123-130] A recent large retrospective cohort study also suggests an association with prescribed opioid dose and suicide risk among Veterans receiving OT for CNCP.[131] Suicide risk is not static, and many factors influence an individual's risk of suicide at any given point in time, as noted in the VA/DoD Suicide CPG.[10] Thus, ongoing assessment of suicide risk is important whether one is initiating, maintaining, or terminating LOT.

There is moderate quality evidence that intensification of monitoring helps mitigate the risk of suicide among patients on LOT. Im et al. (2015) found moderate quality evidence that, at the facility level, patients on LOT within facilities ordering more drug screens than the comparison group were associated with decreased risk of suicide attempt (chronic short-acting opioid group: OR: 0.2, 95% CI: 0.1-0.3; chronic long-acting opioid group: OR: 0.3, 95% CI: 0.2-0.6). In addition, patients on long-acting opioids within the facilities providing more follow-up after new prescriptions were associated with decreased risk of suicide attempt (OR: 0.2, 95% CI: 0.0-0.7).[61]

Some patients on LOT who suffer from chronic pain and co-occurring OUD, depression, and/or personality disorders may threaten suicide when providers recommend discontinuation of opioids. However, continuing LOT to "prevent suicide" in someone with chronic pain is not recommended as an appropriate response if suicide risk is high or increases. In such cases, it is essential to involve behavioral health to assess, monitor, and treat a patient who becomes destabilized as a result of a medically appropriate decision to taper or cease LOT.

Further research is needed to identify strategies for safely managing patients at elevated risk of suicide who demand opioid medications or become further destabilized during tapering.

Recommendation

9. We recommend evaluating benefits of continued opioid therapy and risk for opioid-related adverse events at least every three months.
   (Strong for | Reviewed, New-replaced)

Discussion

Prior to initiating OT, an individualized assessment of potential opioid-related harms relative to realistic treatment goals must be completed. After initiating OT, frequent visits contribute to the appropriate use and adjustment of the planned therapy.

The Work Group recommends follow-up at least every three months or more frequently (see Recommendation 7 and Recommendation 11) due to the balance of benefits and harms associated with this recommendation. Although the 2010 OT CPG recommended follow-up every six months, this

[10] See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk of Suicide. Available at: http://www.healthquality.va.gov/guidelines/MH/srb/

Key Question 7: What is the comparative effectiveness of different risk mitigation strategies for patients either on COT or being considered for COT? a.) Does this differ for patients with history of or current SUD? b.) Does this differ for patients with mental health comorbidities? c.) Does this differ for patients with medical comorbidities?

Summary of Evidence Base

- Our searches identified one systematic review, one retrospective database study, and one prospective cohort study that addressed this question.
  - The systematic review includes 11 studies examining opioid treatment agreement and urine drug testing strategies.[1]
    - Review authors' analysis concluded that weak evidence exists supporting these risk mitigation strategies as effective for reducing opioid misuse among patients receiving chronic opioid therapy (Quality of evidence ratings for outcomes reported in this systematic review: Low to Very low)
    - Conclusions are supported by two meta-analyses (N=426 and N=500, respectively)
  - One retrospective database study investigated the interaction between the degree of individual- and facility-level guideline-recommended opioid care at Veterans Health Administration facilities and patients' risk of attempting suicide.[2]
    - Study authors reported that, at the facility level, adherence to strong care and management practices, including regular drug screening and specialized substance use treatment, was associated with decreased risk of patients attempting suicide. Conversely, high sedative and SNRI co-prescription rates were associated with increased suicide attempt risk among patients receiving long-acting opioid therapy. (Quality of evidence rating: Moderate)
    - Subgroup analysis of patients with comorbid SUD found similar patterns between strong guideline adherence and patients' decreased suicide risk. (Quality of evidence rating: Moderate)
  - One prospective study examined the efficacy of using clinical pharmacist-led guidance teams to provide structured, comprehensive management and risk mitigation services to patients receiving chronic opioid therapy to treat chronic pain due to cancer.[3]
    - Study authors report that, compared to standard of care, treatment directed by clinical pharmacist-led guidance teams was associated with better pain management, improved patient quality of life, and reduced adverse event rates. therapy (Quality of evidence ratings for outcomes reported in this study: Very low)
- Our searches did not identify any systematic reviews that comprehensively addressed the efficacy of other risk mitigation strategies, nor did we locate any eligible randomized controlled trials investigating any risk mitigation strategies of interest among this patient population. The quality of the identified evidence base ranged from Very Low to Moderate, often due to significant methodological issues among included studies.

Table 3. Individual Studies

Study Details	Patients/Interventions	Intervention/Treatment	Outcomes/Results
Reference: Im et al. 2015[2] **Country:** USA **Study Design:** Retrospective database study **Purpose:** To examine associations between the receipt of guideline-recommended care for opioid therapy and risk of suicide attempt. **Quality Rating:** Fair Very large population included; multiple relevant variables included in analysis, but a few relevant potential confounders not included.	**Number of Patients:** 487,462 veterans **Diagnosis:** Not reported; 80.8% received chronic short-acting (CSA) opioids, 19.2% received long-acting (LA) opioids **Age (Years):** Adults aged 18 years and older, mean and range not reported **Gender:** 6.5% female **Inclusion Criteria:** All veteran patients prescribed any short-acting opioids on a chronic basis (chronic short-acting) or any long-acting opioids from the VHA during fiscal year 2010 (FY10) were included in this analysis. Chronic use of short-acting opioids was defined as having at least 90 days of supply in FY10. **Exclusion Criteria:** Not reported	Multivariate, mixed-effects logistic regression analyses were conducted to define the associations between the risk of suicide attempt and receipt of guideline-recommended care at the individual level and rates of use of recommended care at the facility level, while accounting for patient risk factors. Separate analyses were done for patients receiving CSA opioids and patients receiving LA opioids, respectively. Individual-level variables included age, gender, and marital status. Age was categorized into three groups: younger than 31 years old, 31–55 years old, and greater than 55 years old. Physical/mental health status was represented by indicator variables for medical frailty, drug/alcohol/mood disorder, and traumatic brain injury. Binary indicator variables were used to identify whether patients received guideline-recommended care. Facility-level guideline-recommended care delivery rates were also used in the analysis. These rates were calculated for each VHA facility by dividing the number of patients on opioid therapy receiving each guideline recommended service by the total number of patients on opioid therapy within the VHA facility. **Follow-up:** 1 year	**CSA Opioid Therapy: Multivariate Logistic Regression Analysis** At the facility-level, patients prescribed CSA opioid therapy within VHA facilities ordering more drug screens were associated with decreased risk of suicide attempt (OR=0.2, 95% CI: 0.1 to 0.3). SUD subgroup: At the facility-level, SUD-diagnosed patients on CSA opioid therapy within VHA facilities ordering regular drug screens (defined as at least one drug screen for every 90 days of opioid supply) more consistently or providing more SUD specialty treatment/SUD specific pharmacotherapies were associated with decreased risk of suicide attempt (OR=0.3, 95% CI: 0.2 to 0.6). **LA Opioid Therapy: Multivariate Logistic Regression Analysis** At the facility level, the LA opioid therapy group within VHA facilities ordering more drug screens was associated with decreased risk of suicide attempt (OR=0.3, 95% CI: 0.2 to 0.6); in addition, the LA opioid therapy group within VHA facilities providing more follow-up after new prescriptions was associated with decreased risk of suicide attempt (OR=0.2, 95% CI: 0.0 to 0.7), and the LA opioid therapy group within VHA facilities having higher sedative co-prescription rates was associated with increased risk of suicide attempt (OR=20.3, 95% CI: 1.1 to 382.2). SUD subgroup: At the facility-level, SUD-diagnosed group on LA opioid therapy within VHA facilities providing more rehabilitation medicine were associated with decreased risk of suicide attempt (OR=0.3, 95% CI: 0.1 to 0.9), while SUD diagnosed patients within VHA facilities having higher sedative co-prescription rates and providing more SNRIs were associated with increased risk of suicide attempt

obtain UDT prior to initiating or continuing LOT and periodically thereafter. When a patient is referred for SUD treatment or is engaged in on-going treatment there should be close communication between the SUD and pain management providers. The ideal approach is an interdisciplinary format (see Recommendation 16).

For more information, see Appendix B on UDT and confirmatory testing.

Prescribing of Naloxone Rescue and Accompanying Education

Naloxone administration has been identified as a life saving measure following opioid overdose. A systematic review of 22 observational studies provided moderate quality evidence that take home naloxone programs are effective in improving overdose survival and decreasing mortality, with a low rate of adverse events.[108] One meta-analysis of nine studies determined that take home naloxone kits were used approximately nine times within the first three months of follow-up for every 100 individuals trained.[109] Further, studies have shown that naloxone administration has been efficacious whether given by medical personnel or lay people, with more than 26,000 reversals documented by the CDC from 1996-2014.[110,111] In addition, prescription of naloxone rescue and accompanying education has also been found to reduce opioid-related emergency department visits.[112] Distribution of naloxone for reversal is supported by SAMHSA, the American Medical Association (AMA), and other medical societies, and is facilitated through the VA via Pharmacy Benefits Management. Clinical efficacy has been established for its use on short-acting opioids, but not for its use on long-acting opioids such as methadone or exceptionally potent opioids.[108]

Synthetic opioids such as fentanyl analogs, potent opioid receptor agonists, are responsible for a recent rise in death rates. Fentanyl analogs that may be used to create counterfeit opioid analgesic pills can cause a toxidrome characterized by significant CNS and profound respiratory depression requiring multiple naloxone doses for reversal.[113]

Patients at High Risk for Opioid Use Disorder

Those patients receiving opioid analgesics who do not meet DSM-5 criteria for OUD may benefit from an alternative management strategy: close follow-up and CBT. Jamison et al. (2010) randomized patients at high-risk for OUD (as measured by standard rating scales) to receive either standard pain management or close follow-up with CBT for pain.[114] Both of these groups were compared to a low-risk, chronic pain control group receiving standard management. The authors report that, compared to a matched high-risk group receiving standard care, patients receiving additional monitoring and CBT exhibited significantly reduced illicit substance use over six months (percentage of patients with positive drug misuse index scores: 73.7% versus 26.3% versus 25.0%; $p<0.01$). At six months, there was no difference between the high-risk group receiving close follow-up and the low-risk group receiving standard therapy. Authors also reported that pain perception was less in the high-risk group receiving additional monitoring and behavior therapy; however, analysis of activity interference reporting reflected no significant difference between study groups.

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PART 3 — Patient input and its disposition (supports Policy Idea 3.1)

ID	Source	Description
H-09	CPG p. 32	Focus group held December 14, 2015; Work Group’s acknowledgment of small, non-representative sample; Focus Group Concepts table A–G
H-10	CPG p. 123	Appendix F methods: six patients and two family caregivers; facilitator from The Lewin Group
H-11	CPG p. 124	Appendix F findings: shared decision-making and treatment-modification themes
H-12	CPG p. 125	Appendix F findings: education regarding treatment changes and tapering; seamless transitions in care
H-13	CPG p. 63	Focus-group input cited in the tapering discussion (sole recommendation-adjacent use in the guideline body)

CPG = Clinical Practice Guideline | ESR = Evidence Synthesis Report

highlighted and made explicit due to their potential to influence a recommendation's implementation.[75,76] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals with an *a priori* set of assumptions or hypotheses and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership, along with the OT CPG Work Group, held a patient focus group on December 14, 2015, at the Washington DC VA Medical Center. One additional family caregiver was interviewed separately at a later date. The aim of the focus group and interview was to further the understanding of the perspectives of patients receiving OT within the VA and/or DoD healthcare systems. The focus group and interview explored patient perspectives on a set of topics related to management of OT in the VA and DoD healthcare systems, including knowledge of OT and other pain treatment options, delivery of care, and the impact of and challenges with OT and chronic pain.

It is important to note the focus group was a convenience sample and the Work Group recognizes the limitations inherent in the small sample size. Less than 10 people were included in the focus group consistent with the requirements of the federal Paperwork Reduction Act, 1980. The Work Group acknowledges that the sample of patients included in this focus group may not be representative of all VA and DoD patients on or being considered for OT for chronic pain. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to pain care in the VA and DoD and the patients' broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus group and interview. These limitations, as well as others, were considered as the information collected from the discussion was used for guideline development. Recruitment for participation in the focus group was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facility at which the focus group took place.

The following concepts are ideas and suggestions about aspects of care that are important to patients and family caregivers and that emerged from the discussion. These concepts were needed and important parts of the participants' care and added to the Work Group's understanding of patient values and perspectives. Additional details regarding the patient focus group methods and findings can be found in Appendix F.

OT CPG Focus Group Concepts	
A.	Using shared decision making, consider all treatment options and develop treatment plan based on the balance of risks, benefits, and patient-specific goals, values, and preferences
B.	Modify treatment based on patient response, considering patient-specific goals, values, and preferences
C.	Involve family caregivers in accordance with patient preferences and maintain open, trusting, and respectful relationship with patients and family caregivers
D.	Educate patients regarding treatment plan, alternative treatment options, and monitoring
E.	Within and between healthcare systems, work with appropriate providers to ensure continuity of high quality care
F.	Organize treatment to encourage patient adherence and participation
G.	Acknowledge and minimize effects of potential medical error and take action to prevent future medical error

F. Conflict of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in

Appendix F: Patient Focus Group Methods and Findings

A. Methods

On December 14, 2015, as part of the effort to update this CPG, the VA and DoD Leadership, along with the OT CPG Work Group, held a patient focus group at the Washington DC VA Medical Center. Focus group participants included six patients and two family caregivers. One additional family caregiver was interviewed separately at a later date.

The aim of the focus group and interview was to further the understanding of the perspectives of patients receiving LOT within the VA and/or DoD healthcare systems, as these patients are most affected by the recommendations put forth in the updated OT CPG. The focus group and interview explored patient perspectives on a set of topics related to management of OT in the VA and DoD healthcare systems, including knowledge of OT and other pain treatment options, delivery of care, and the impact of and challenges with LOT.

Participants for the focus group were recruited from the pain clinics at the Walter Reed National Military Medical Center and the Washington DC VA Medical Center. Patient focus group participants were not intended to be a representative sample of VA and DoD patients who have experienced LOT. However, recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the guideline development process. Patients were not incentivized for their participation or reimbursed for travel expenses.

The OT CPG Champions and Work Group developed a set of questions to help guide the focus group and interview. The facilitator from Lewin led the discussion using interview questions prepared by the Work Group as a general guide to elicit the most important information from the patients regarding their experiences and views about their treatment and overall care. Given the limited time and the range of interests and expressiveness of the participants, not all of the listed questions were addressed.

At the time of the focus group, three patients were receiving care in the DoD healthcare system, two patients were receiving care in the VA healthcare system, and one patient was receiving care from a private pain center. Some of these patient participants had transitioned between multiple care settings, including from VA to DoD, from DoD to VA, and from a governmental healthcare setting to a private healthcare setting. Two patients stated that they were currently on LOT for pain. Four patients stated that they had previously been on LOT, but have since transitioned to other treatments for pain.

The following concepts are aspects of care that are important to patients and family caregivers that emerged from the focus group discussion and the interview. Each of these themes was an important and needed aspect of participants' healthcare.

B. Patient Focus Group Findings

Using shared decision making, consider all treatment options and develop treatment plan based on the balance of risks, benefits, and patient-specific goals, values, and preferences

- Identify patient-specific goals associated with LOT (main goals of these focus group participants included returning to work, minimizing pain, maintaining a functional life, avoiding invasive medical procedures, and getting off opioids)
- Discuss and consider all pain management options (non-pharmacotherapy and non-opioid pharmacotherapy) prior to starting LOT; do not default to prescribing opioids
- Use shared decision making to develop an individualized treatment plan; discuss pros and cons (e.g., benefits, risks, side effects) of each treatment option (including non-opioid treatment options) in conjunction with each patient's goals, priorities, values, and preferences
- Maintain focus on patient goals throughout treatment, including any changes in those goals over time

Modify treatment based on patient response, considering patient-specific goals, values, and preferences

- Be prepared to adjust or otherwise change treatment (e.g., tapering opioids) subject to patient response, preferences, and changes in priorities and goals; convey this flexibility and support the patient and support him/her during the change in treatment
- Do not continue to prescribe opioids when patients express reluctance to take them or do not adhere; continue to understand patient needs and preferences and adapt treatment accordingly
- Take time to develop a thorough understanding of patient needs and capabilities; develop an individualized treatment plan; be accountable for adverse outcomes
- Even after LOT is initiated, continue to discuss and consider all pain management options (non-pharmacotherapy and non-opioid pharmacotherapy)
- Carefully consider side effects during monitoring and adjust treatment in order to minimize side effects (e.g., depression, weight gain, headaches, nightmares, problems with intimacy, paresthesias) pursuant to individual patient preferences

Involve family caregivers in accordance with patient preferences and maintain open, trusting, and respectful relationship with patients and family caregivers

- Foster family, including family caregiver, involvement in shared decision making and support in accordance with patient preferences and in a way that is beneficial to the patient
- Always treat patients and family, including family caregivers, with respect and support
- Build and maintain trust, respect, and support in relationship with the patient and family, including family caregivers
- Ensure the patient has the capability to engage in shared decision making; recognize that patients who are in pain or who are taking opioids or other powerful medications may be in

suboptimal condition to make informed decisions on their own and may benefit from involvement of knowledgeable family members, including family caregivers

Educate patients regarding treatment plan, alternative treatment options, and monitoring

- Clinicians should be proactive and responsive in providing necessary clinical information in a manner comprehensible to patients and family caregivers; acknowledge that patients will seek and acquire information from other sources (especially the Internet) and encourage patient proactivity
- When prescribing opioids, provide in-depth and patient-specific education on medication (e.g., side effects, dosing, administration, storage, safety, disposal, take back programs) during medical visits in conjunction with distributing or otherwise enabling access to educational materials
- Provide necessary information regarding changes in treatment; discuss tapering and risks of self-tapering as necessary; recognize and address the challenges for patients on OT, including tapering
- Explain/provide education to patients as to why doctors use monitoring practices such as UDT when patients are using opioids; do not simply order the tests without such explanation

Within and between healthcare systems, work with appropriate providers to ensure continuity of high quality care

- Consult with other providers (e.g., psychologists, physical therapists) and patient advocates as appropriate, especially when patients express the need for more information or other clinical support
- Provide seamless transitions in opioid treatment and other pain management within and between VA, DoD, and any other healthcare systems; patients should not have to encounter abrupt changes in treatment regimens moving from one system to another or have to "start all over" when moving to another system
- Continue transformation of pain management

Organize treatment to encourage patient adherence and participation

- Facilitate appointment scheduling for days and times that fit the patient's needs (e.g., try to avoid patient work days where possible, schedule multiple provider appointments on same day rather than multiple days)
- Facilitate prescription refills and patient visits for refills in a way that fits the patient's needs, lifestyle, and schedule, while maintaining safe prescribing practices

Acknowledge and minimize effects of potential medical error and take action to prevent future medical error

- Acknowledge instances of potential medical error or other instances in which patient outcomes from previous medical procedures were less than desirable or expected (including experiences

be taken into consideration when determining the balance of risks and benefits of OT, recognizing that multiple risk factors increase cumulative risk:[172,173]

- Concomitant use of medications that increase risk of overdose
- Co-occurring medical or mental health conditions that increase risk
- Concerns about OUD or other SUD
- Patient adherence with opioid safety measures and opioid risk mitigation strategies
- Patient non-participation in a comprehensive pain care plan
- Prescribed dose higher than the maximal recommended dose (which increases risk of adverse events) (see Recommendations 10-12)
- Pain condition not effectively treated with opioids (e.g., back pain with normal magnetic resonance imaging [MRI]; fibromyalgia)
- Improvement in the underlying pain condition being treated
- Lack of clinically meaningful improvement in function
- Unmanageable side effects

When there is strong concern for diversion, opioids should be discontinued. For all patients, the prescribing clinician should regularly inquire about the patient's preference to taper OT to a reduced dose or discontinuation and explore ambivalence. OT should be tapered when patients voice their preference to reduce dosage and/or discontinue LOT.

There is large variation in patient preferences regarding continuing versus tapering OT and regarding the various processes that can be used when tapering opioids. Participants in the patient focus group expressed concern that when patients are receiving LOT, they may experience impaired judgement regarding decisions about opioid discontinuation due to the reinforcing nature of OT. Patients, therefore, may benefit from the outside perspective of their family members and healthcare providers. Such involvement should occur in accord with patient's preferences and within applicable privacy requirements (see Patient Focus Group Methods and Findings).

Low frequency of follow-up in primary care and limited access to comprehensive interdisciplinary specialty pain, rehabilitation, mental health, and addiction services may be barriers to tapering LOT that may need to be addressed.

Assessment/Follow-up

A biopsychosocial assessment including evaluation of medical, psychiatric, and co-occurring substance use conditions, as well as the patient's social support system, should be completed prior to the initiation of an opioid taper. The risks and benefits of the current opioid regimen should be weighed with the risks and benefits associated with a reduction in opioid dose. Periodic re-evaluation of risks and benefits coupled with a biopsychosocial assessment should occur when implementing an opioid taper and on follow-up. The frequency and type of follow-up is determined by risk assessment performed by the healthcare team. Follow-up should occur within a range of one week to one month after any opioid dosage change. Each follow-up interaction with the patient is an opportunity to provide education about self-management

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PART 4 — Monitoring and the evaluation gap (supports Policy Idea 5.1)

ID	Source	Description
H-14	CPG p. 17	Opioid Safety Initiative indicators tracked prescribing metrics rather than patient outcomes
H-15	CPG p. 67	Future Research section: outcome evidence on tapering processes still needed
H-16	CPG p. 66	Consensus-based taper parameters (5–20% every four weeks) offered where the evidence review found none
H-17	ESR p. 332	Literature searches conducted by ECRI Institute information specialists

CPG = Clinical Practice Guideline | ESR = Evidence Synthesis Report

This public health issue, which has been labelled an epidemic,[22] became a focus of the President's National Drug Control Strategy in 2010 and has since remained a focus. Two main goals introduced in the 2010 strategy included curtailing illicit drug consumption in America and improving the health and safety of the American people by reducing the consequences of drug abuse.[23] The 2015 strategy, and an accompanying presidential memorandum on preventing prescription drug abuse and heroin use, released in October 2015, encouraged the improvement of health and safety using evidence-based methods by calling for change in a number of key areas including preventing drug use in communities, seeking early intervention opportunities, and integrating SUD treatment and supporting recovery.[24,25]

With the passage of the Patient Protection and Affordable Care Act (PPACA) in March 2010, the Interagency Pain Research Coordinating Committee was created to coordinate pain research efforts throughout federal government agencies. The Committee was tasked with summarizing advances in pain care research, identifying gaps in research, and developing recommendations regarding ways to minimize duplicative efforts, disseminate pain care information, and expand public/private research partnerships and collaborations. The Committee published the National Pain Strategy in March 2016 in response to the call from the National Academy of Medicine to increase awareness of pain as a significant public health issue in the U.S.[3] The strategy made recommendations in a number of areas including prevention and care, professional education and training, and population research. The plan is aimed at decreasing the prevalence of all types of pain (acute and chronic) in the U.S., as well as the disability and morbidity associated with pain.[26]

Government agencies, including the VA, DoD, and Substance Abuse and Mental Health Services Administration (SAMHSA), have also launched initiatives to improve the study and treatment of pain and adverse events associated with opioid analgesics such as OUD and overdose.[27] By August 2013, the VA deployed the Opioid Safety Initiative (OSI) requirements to all Veterans Integrated Service Networks (VISNs) with the aim of ensuring opioids are used in a safe, effective, and judicious manner. The goals of the OSI related to such topics as increased education, monitoring, use of safe and effective prescribing and management methods, tool development, collaboration, and use of alternative pain treatment. The OSI uses the Veterans Health Administration (VHA's) electronic health record to identify patients who may be high-risk for adverse outcomes with use of opioids and providers whose prescribing practices do not reflect best evidence so that patient care can be improved. The OSI requirements include specific indicators (e.g., the number of unique pharmacy patients dispensed an opioid, the unique patients on LOT who have received UDT).[28] As part of the OSI, the VA launched the Opioid Overdose Education and Naloxone Distribution (OEND) program, which was implemented as a risk mitigation strategy aimed at reducing deaths from opioid overdose. The program components included education and training regarding the following topics: opioid overdose prevention, recognition, and rescue response; risk mitigation strategies; and issuing naloxone kits, which can be used as an antidote to opioid overdose.[29,30]

Other initiatives are aimed at improving the safe use of opioids, including the OSI Toolkit and the patient guide *Taking Opioids Responsibly for Your Safety and the Safety of Others: Patient Information Guide on Long-term Opioid Therapy for Chronic Pain*. The OSI Toolkit was developed to provide clinicians with materials to inform clinical decision-making regarding opioid therapy and safe opioid prescribing.[31] The toolkit materials can be found at the following link:

Naloxone

Overdose education should be provided and naloxone should be offered as an antidote to all patients at risk for an opioid overdose including those who are in the process of tapering. During and following an opioid taper, patients may still be using opioids from other sources such as saved opioids, other prescribers, friends and family, as well as illicit sources. Continued surveillance for OUD and assessment for naloxone is suggested in patients who are no longer on opioids but who remain at risk for opioid use from unknown sources. For more information, see Recommendations 7-9.

Future Research

Additional research is needed to identify the opioid tapering processes that are associated with the best patient outcomes among a broad range of domains including general functioning, psychosocial functioning, mood, pain related disability, and adverse outcomes assessed in the short, medium, and long-term.

Recommendation

16. We recommend interdisciplinary care that addresses pain, substance use disorders, and/or mental health problems for patients presenting with high risk and/or aberrant behavior. **(Strong for| Reviewed, New-replaced)**

Discussion

A variety of high-risk medication-related behaviors (e.g., early refills, lost or stolen medications, problematic findings on urine tests) may suggest the presence of SUD (also known as opioid addiction, abuse, or dependence). Non-adherence to treatment plans or repeated failure to show for clinic appointments can add to the challenge of safely providing LOT in the primary care setting. The presence of co-occurring SUD or psychiatric conditions in some patients can make prescribing LOT an overwhelming problem for primary care providers. Chronic pain is a complex human experience influenced by physical, psychological, and social factors. Multidisciplinary care that addresses these influences is helpful for all patients, but is absolutely essential when pain is accompanied by co-occurring conditions, impaired function, or psychological problems.

Low quality evidence supports the benefits of providing brief behavioral interventions and close monitoring to patients at high risk for prescription opioid misuse.[114] Some evidence suggests that patients referred to highly structured opioid-renewal programs that provide patients with frequent UDT monitoring, frequent clinic visits, smaller quantities of medications, and ongoing counseling/education is helpful for patients and primary care providers. Meghani et al. (2009) found that high-risk medication-related behaviors resolved in 45.6% of patients managed in a pharmacist-run opioid renewal clinic.[176] Although the confidence in the quality of the evidence was low, the Work Group's determination that the benefits of interdisciplinary care for patients with pain and other comorbidities (e.g., SUD, mental health problems) contributed to a strong recommendation.

Consider referring patients with co-occurring substance use or psychiatric conditions to addiction medicine/psychiatry or other behavioral health specialists. Coordination of care between pain care and other specialty care, including SUD clinicians, is advised. If structured comprehensive programs are not available, coordination among individual healthcare providers is essential to address the full range of high-

The characteristics that will determine the speed of tapering include opioid dose, duration of therapy, type of opioid formulation, and co-occurring psychiatric, medical, and substance use conditions. The tapering treatment plan should be individualized and should address the pace of tapering, setting of care, and frequency of follow-up. When determining the pace of opioid tapering, factors that would suggest a more gradual taper include higher opioid dose and longer duration of OT; factors that would suggest a more rapid taper include non-adherence to the treatment plan and escalating high-risk medication-related behaviors. When safety permits, gradual tapers are often better tolerated. In addition, for some patients, pauses in the taper for weeks or months may allow the patient time to acquire new skills for management of pain and emotional distress while also allowing time for neurobiological equilibration.

The rate of taper takes into account many factors that include initial dose, formulations available, and risk factors that increase harm. A gradual taper over months or even years for patients starting on very high opioid doses involves reducing by 5-20% every four weeks. In some patients, a faster taper may be needed when risks are too high to consider a gradual taper; consider tapering the dose by 5-20% per week in this patient population.

When it is determined that patient risks are significantly high to warrant a rapid taper over a period of days or weeks, then specialty consultation should be obtained to determine the rate of taper and resources needed. These patients will need frequent follow-up and reevaluation of SUD, mental health, and/or co-occurring medical conditions with every dose change.

Patients Receiving Very High Dose Opioid Therapy

For patients currently prescribed ≥90 mg MEDD, a comprehensive assessment that recognizes the increased risk of high dose OT should be performed. Tapering to a reduced dose or tapering to discontinuation should be pursued when clinically meaningful functional benefit is not demonstrated or when significant risk factors in addition to the prescribed opioid dose are present. It should be recognized that elevated dose alone poses increased risk of overdose, overdose death, adverse effects, and the development of OUD. Assessing clinically meaningful functional benefit should be individualized and incorporate the use of SMART goals and considered in the context of patient-specific goals, values, and preferences (see table Guide in Setting SMART Goals).

Mental health and SUD comorbidities that were previously unrecognized or that may worsen should be assessed and addressed with an interdisciplinary approach. Interdisciplinary care including mental health, rehabilitation, and SUD treatment services may be necessary to support the tapering process. Use of MAT, which includes behavioral approaches, should be offered for patients in whom a diagnosis of OUD is made (see the VA/DoD SUD CPG).[13]

[13] See the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. Available at: http://www.healthquality.va.gov/guidelines/mh/sud/index.asp

Appendix A: Literature Search Methods

Resources Searched

ECRI Institute information specialists searched the following databases for relevant information. Search terms and strategies for the bibliographic databases appear below.

Name	Search Dates	Platform/Provider
Agency for Healthcare Research and Quality (AHRQ)	Searched November 23, 2015	U.S. Department of Health & Human Services
Centers for Disease Control and Prevention (CDC)	Searched November 30, 2015	www.cdc.gov
Cochrane Library	Searched November 5, 2015	John Wiley & Sons, Ltd.
EMBASE (Excerpta Medica)	January 1, 2009 on	
Google	Searched November 23, 2015	www.google.com
Healthcare Standards (HCS)	Searched November 30, 2015	ECRI Institute
Medline	January 1, 2009 on	OVID Technologies, Inc.
National Guideline Clearinghouse (NGC)	Searched November 30, 2015	Agency for Healthcare Research and Quality (AHRQ)
National Institute for Health and Care Excellence (NICE)	Searched November 23, 2015	National Institute for Health and Care Excellence
PsycINFO	January 1, 2009 on	OVID Technologies, Inc.
PubMed (In-process, Publisher, and PubMedNotMeSH records)	Searched October 22, 2015 and January 11, 2016	National Library of Medicine (NLM)

Hand Searches of Journal and Gray Literature

Journals and supplements maintained in ECRI Institute's collections were routinely reviewed. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also screened. Other mechanisms used to retrieve additional relevant information included feedback and recommendations from work group members and review of bibliographies/reference lists from peer-reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.)

Topic-specific Search Terms

The vocabulary presented in this table includes controlled vocabulary and free-text keywords for bibliographic database searches performed in EMBASE, Medline, and PsycINFO. Strategies for selected databases follow this table.